

# Asymmetric septal hypertrophy and propranolol treatment in a case of Ullrich-Noonan syndrome

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**SUMMARY** A 4-year-old boy with the Ullrich-Noonan syndrome is described. Asymmetric septal hypertrophy was diagnosed by echocardiography and confirmed at cardiac catheterisation. The aortic subvalvar gradient was reduced from 56 mmHg to 10 mmHg with intravenous propranolol. Relatives of patients with the syndrome should be screened by echocardiography in the hope that the early detection of asymmetric septal hypertrophy and its treatment with propranolol may reduce the likelihood of sudden death.

The clinical and cardiovascular manifestations in patients with the Ullrich-Noonan syndrome have been extensively reviewed (Nora *et al.*, 1974). Patients, who may be of either sex, have a normal karyotype, but have an appearance typical of Turner's syndrome, very short stature, webbing of the neck, and a typical facies. The most common cardiac abnormality is valvar pulmonary stenosis with or without an atrial septal defect. Less frequently, stenosis of the peripheral branches of the pulmonary arteries, aortic stenosis, ventricular septal defect, the tetralogy of Fallot, persistent ductus arteriosus, and coarctation of the aorta may occur. Asymmetric septal hypertrophy (ASH) has been reported more recently (Ehlers *et al.*, 1972). Nora *et al.* (1974) reported 2 cases of isolated ASH, 5 associated with pulmonary stenosis, and 1 associated with coarctation of the aorta. Phornphutkul *et al.* (1973) reported 1 case of ASH and 2 cases of non-obstructive cardiomyopathy. Here we report a further example of the syndrome in whom the cardiac abnormalities were ASH and aortic stenosis.

## Case report

A 4-year-old white boy with a clinical diagnosis of the Ullrich-Noonan syndrome was referred for cardiological investigation. His mother had been previously diagnosed at another hospital as having the Ullrich-Noonan syndrome associated with ASH. She had recently died as a result of accidental electrocution. Three of the mother's sibs had heart disease. One died when 2 hours old, one died aged

3 weeks, and one had an aortic valve replacement for aortic stenosis when aged 38. The cause of death of the youngest 2 was given as congenital heart disease. Our patient has a co-maternal half sister who is cardilogically normal.

Our patient complained of slight shortness of breath on vigorous exercise but was otherwise asymptomatic. His milestones were normal and he was not mentally retarded. His height was below the third centile and his weight was at the fiftieth centile. He had a small mouth, broad nose, widely spaced eyes, a left epicanthic fold, and slight right ptosis. He had prominent, low set ears and a low hairline at the neck. There was no webbing of the neck or pectus excavatum. His right testis was not fully descended. Cardiac examination revealed a normal heart size with a left ventricular impulse, a late systolic murmur maximal at the left sternal edge and a fourth heart sound. His buccal smear was chromatin negative and he had a normal male karyotype. His electrocardiogram showed a mean frontal plane axis of minus 110 degrees with large R waves in leads aVR and aVL and a QS pattern in lead V6 with a deep Q wave in V5 (Fig. 1). Chest x-ray film was normal. An echocardiogram (Fig. 2) disclosed septal hypertrophy, the septal thickness being 1.3 cm just below the level of the mitral valve. There was systolic anterior movement of the mitral valve and the anterior leaflet of the mitral valve impinged upon the septum in diastole. The pressures recorded at cardiac catheterisation are shown in the Table, the left ventricular end-diastolic pressure being 12 mmHg with a gradient of 56 mmHg within the left ventricle and an aortic

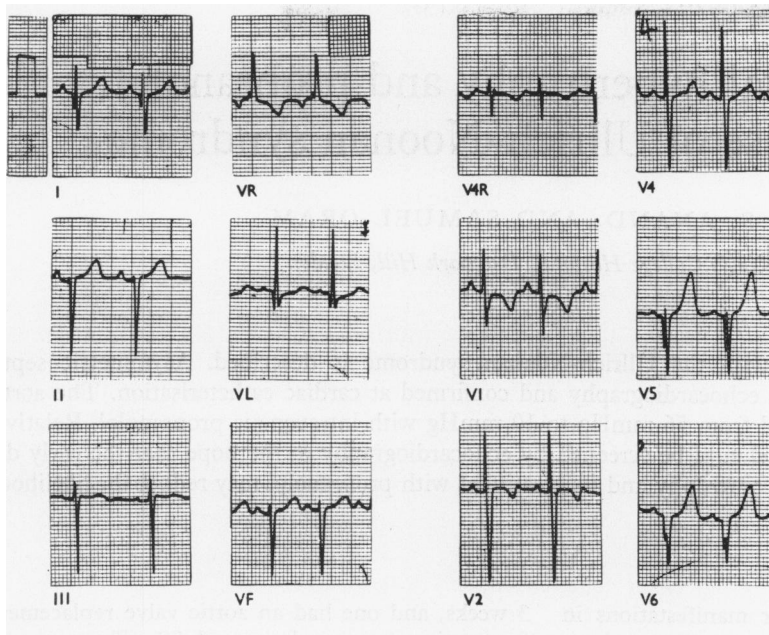


Fig. 1 Electrocardiogram (paper speed 25 mm/s). See text.

valvar gradient of 44 mmHg. Though the foramen ovale was crossed, measurement of oxygen saturation did not reveal any arteriovenous shunt.

The absence of an intra-aortic pressure gradient excluded coarctation. No pressure gradient was found in any branch of the pulmonary arteries.

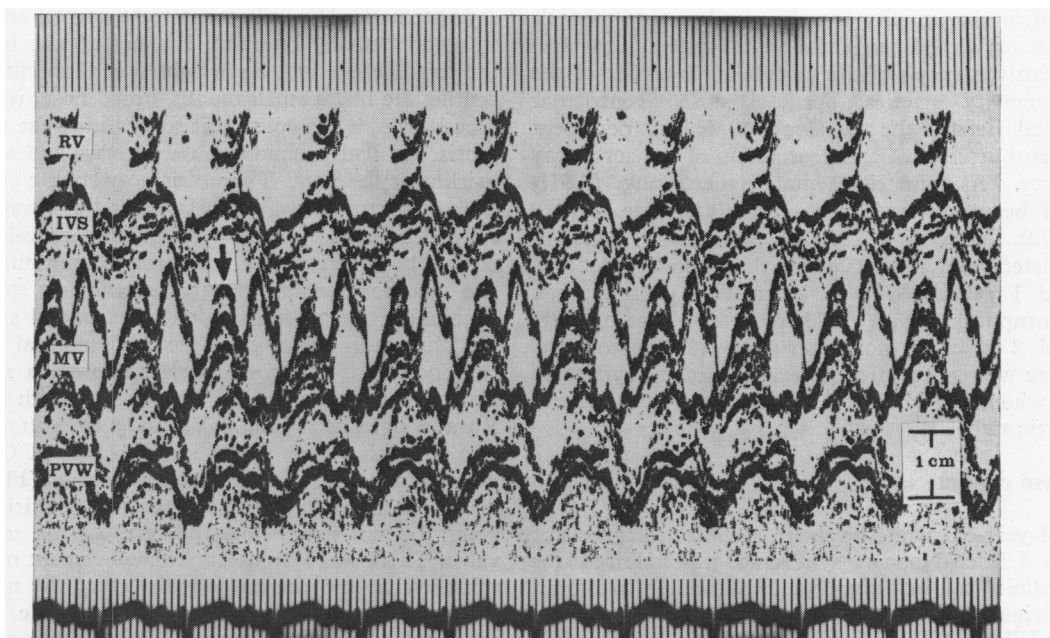


Fig. 2 M-mode echocardiogram (paper speed 50 mm/s) at the level of the anterior leaflet of the mitral valve. There is prominent systolic anterior movement of the anterior leaflet which has a reduced diastolic closure rate and abuts on to the septum in diastole. RV, right ventricle; IVS, interventricular septum; MV, mitral valve; PVW, posterior ventricular wall.

Table Pressures recorded at cardiac catheterisation (mmHg)

Right atrium	8 mean	Aorta	100/64
Right ventricle	28/0	Left ventricle	200/12
Pulmonary artery	28/10	Left ventricle (after propranolol)	144/12
Pulmonary artery branches	28/10	Subvalvar gradient	56
Left atrium	8 mean	Aortic valvar gradient	44

Left ventricular angiography showed septal hypertrophy, trabeculation, and mitral regurgitation (Fig. 3). After the administration of propranolol 0.8 mg (0.05 mg/kg) intravenously, the subvalvar gradient was reduced to 8 mmHg, with the aortic valvar gradient also being reduced to 10 mmHg. Biopsy of the right ventricle was histologically normal; biopsy of the left ventricle was technically unsuccessful. The patient was discharged home taking propranolol 5 mg t.d.s. Three weeks later the patient was asymptomatic and his murmur had decreased in intensity. The echocardiogram was repeated 3 months later, propranolol having been withdrawn for 48 hours. The degree of systolic anterior movement of the mitral valve was less than that of the control recording despite temporary withdrawal of treatment. The administration of propranolol 0.8 mg intravenously produced a further slight reduction in systolic anterior movement.

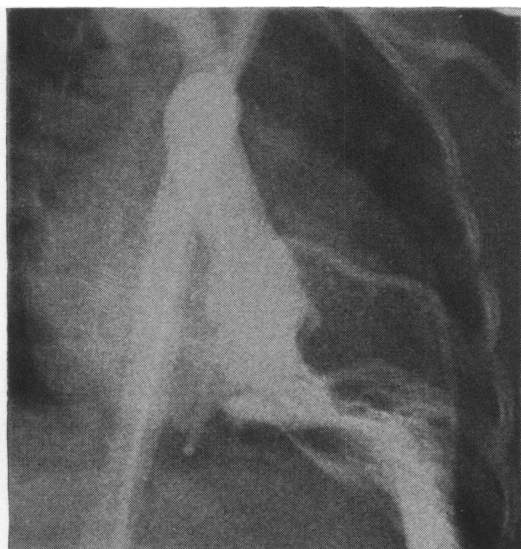


Fig. 3 Left ventricular angiogram in the right anterior oblique position illustrating severe septal hypertrophy and mitral regurgitation.

## Discussion

We report a case of the Ullrich-Noonan syndrome associated with ASH investigated by echocardiography, left and right heart catheterisation, and right ventricular biopsy. The proven concurrence of ASH with the Ullrich-Noonan syndrome in the mother of our patient strongly suggests that his ASH was inherited as a manifestation of this syndrome.

The reduction of the outflow tract gradient achieved with propranolol in this patient is similar to that found in isolated ASH (Goodwin and Oakley, 1972). The echocardiographic findings were typical of ASH. It is of interest to note that the extent of the systolic anterior movement, and hence the outflow gradient, was reduced after treatment with propranolol for three months despite temporary withdrawal of the drug.

It has been suggested that a superior frontal plane QRS axis in the Ullrich-Noonan syndrome indicates pulmonary stenosis (Rasmussen and Sørland, 1973). We found such an axis but no pulmonary stenosis. However, the presence of a QS pattern in lead V6 and an R wave in lead aVL is compatible with ASH (Bahl and Massie, 1972).

Septal hypertrophy has not been the most frequent association with the Ullrich-Noonan syndrome in the patients so far reported, but since many of these have been investigated only by right heart catheterisation ASH would not necessarily have been suspected. It is possible that the pulmonary stenosis reported in some patients may have resulted from a gradient in the outflow tract of the right ventricle caused by septal hypertrophy. The exact incidence of ASH among patients with the syndrome, and their families can be conveniently determined by echocardiography. It may be that ASH is the common denominator in a group of genetically determined disorders, of which the Ullrich-Noonan syndrome is one.

We have shown a favourable haemodynamic and symptomatic response to propranolol in a patient with the Ullrich-Noonan syndrome. The echocardiographic examination of similar patients and their relatives may lead to early diagnosis of ASH. Treatment with propranolol may in turn favourably affect the natural history of affected individuals, perhaps even reducing the incidence of sudden death, as the presence of congenital heart disease significantly affects mortality (Nora *et al.*, 1974).

We would like to thank Dr P. R. Clay for referring this patient to us.

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